Resource for Individuals Living with Multiple Endocrine Neoplasia

Multiple Endocrine Neoplasia Type 2

Overview

Multiple endocrine neoplasia type 2 (MEN2) is a rare genetic condition that leads to the development of cancers as well as benign tumors of the endocrine system. It includes three clinical subtypes: MEN2A (90% of MEN2 families), MEN2B (5%) and familial medullary thyroid carcinoma (FMTC). MEN2 is due to mutations in the *RET* gene.

Associated Cancers of Multiple Endocrine Neoplasia Type 2

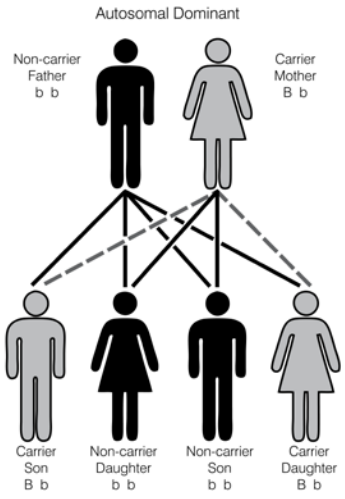
Tumor Type	MEN2A Risk	MEN2B Risk	FMTC Risk
Medullary thyroid carcinoma	~95-100%	~100%	~100%
Pheochromocytoma	50%	50%	Not increased

In addition to increased risks for certain cancers and tumors, individuals with MEN2 may also have other features, such as:

- Primary hyperparathyroidism (PHPT) affects approximately 20-30% MEN2A patients
- Ganglioneuromas of the GI tract and mucosal neuromas are present in nearly all individuals with MEN2B

Genetics and Inheritance of Multiple Endocrine Neoplasia Type 2

MEN2 is due to a change, called a mutation, in a gene called *RET*. Genes are the instructions for the body; they provide the cell with information about how to grow, develop and perform its normal functions. When a gene's code contains a mutation, the normal cell function is impaired or changed. Thus in some instances gene mutations can lead to disease. Each person has two copies of every gene, including the *RET* gene. One copy is inherited from their mother, and one copy is inherited from their father. A mutation in a single copy of the *RET* gene leads to the increased risk of cancer as seen in MEN2.



MEN2 can be passed down through the family by both men and women; there is a 50% (1 in 2) chance that a person with MEN2 will pass the mutation in the *RET* gene to each of their children. This is called autosomal dominant inheritance.

Genetic testing is available to help identify whether an individual has a mutation in the *RET* gene. If a mutation is found, this confirms the diagnosis of MEN2 and allows other at-risk relatives to be tested for the specific *RET* mutation. Sometimes genetic testing will not find a mutation in the *RET* gene in someone with features suggestive of MEN2. This may be explained by limitations in current technology (the person may still carry an undetectable mutation) or another gene may be responsible for the features in the family. A genetics professional can help determine if genetic testing for other genes is warranted.

Medical Management
For individuals with MEN2 syndrome, specialized cancer prevention and early detection guidelines are available to address the increased cancer risks. These interventions can include a range of recommendations and options, such as regular screening, preventive surgery and certain medications.

The National Comprehensive Cancer Center Network provides regularly updated guidelines for management of individuals with MEN2. When possible, individuals with MEN2 should seek management with physicians or centers who are experienced with this condition.

When to Consider Evaluation for Multiple Endocrine Neoplasia Type 2
Reviewing family history information with a genetic counselor can help determine the chance that a family has MEN2 or other genetic conditions that may predispose family members to cancers.
Features in the family history which may suggest MEN2:

- Family member with a confirmed mutation in the *RET* gene
- Individuals with medullary thyroid cancer at a young age
- Individuals with an endocrine tumor and a family history of endocrine tumors

Genetic Counseling
While mutations in the *RET* gene are responsible for causing MEN2 in families, other conditions (and therefore other genes) may appear clinically similar to MEN2. In addition, in many families the cancer may be due to a combination of genetic and environmental factors. For this reason, a detailed review of the family history by a genetics professional is important before pursuing any type of genetic testing. Genetic test results can be complicated and are most useful when interpreted by a genetics professional in the context of an individual's complete personal and family history.

It is important to consider both the pros and cons of genetic testing before pursuing such tests. A genetic counselor can help to identify and explain issues that should be considered regarding genetic testing. A genetic counselor also can help determine which, if any, genetic tests may be helpful for a family.

To locate a genetic counselor near you, please visit www.nsgc.org and click on the 'Find a Genetic Counselor' link.

Genetic Discrimination
The Genetic Information Nondiscrimination Act (GINA) was signed into federal law in 2008. GINA prohibits health insurers and most employers from discriminating against individuals based on genetic information (including the results of genetic tests and family history information). According to GINA health insurance companies cannot consider genetic information to be a preexisting condition, nor can they use it to make decisions regarding coverage or rates. GINA also makes it illegal for employers to use genetic information in making decisions about hiring, firing, promotion, or terms of employment. It is important to note that GINA does not offer protections for life insurance, disability insurance, or long-term care insurance. More information about GINA can be found by contacting a local genetic counselor or by visiting www.ginahelp.org.

Resources

- Moline J and Eng C. Multiple endocrine neoplasia type 2: An overview. *Genetics in Medicine* 2011;9;755-764.
- National Comprehensive Cancer Network, NCCN Clinical Practice Guidelines in Oncology Multiple Endocrine Neoplasia, Type 2, v.1.2011 retrieved December 12, 2011, from www.nccn.org